REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 10-13 and 16-18 are pending after entry of the amendments set forth herein.

Claims 10-13 and 16-18 were examined. Claims 10-13 were rejected. Claims 16-18 were withdrawn from consideration. No claims were allowed.

Claims 10 and 13 are amended. Support for these amendments is found in these claims as originally presented.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

No new matter has been added.

Claims 16-18 Considered Independent and Distinct Inventions

The Office indicated that newly presented claims 16-28, which recited that composition further comprises a biocompatible carrier (claim 16) which carrier can be a hydrogel (claim 17) and can be resorbable (claim 18), is not understood.

Nevertheless, applicants regard these claims as withdrawn.

Withdrawal of Obviousness-type Double Patenting Rejection

Acceptance of the Terminal Disclaimer and withdrawal of this rejection is gratefully acknowledged.

Rejections under §112, ¶2

Claim 10

Claim 10 was rejected for recitation of "a domain that mimics cell binding by collagen." This rejection is respectfully traversed as applied and as it may be applied to the amended claim.

As noted in the prior response, the language present in the original claim is the same language present in multiple issued claims based on the parent applications. Applicants amended in the last response to use language that is also present in these same claims.

Applicants have now amended claim 10 so that it tracks exactly the same language that appears in the claims that issued from the parent applications. Exemplary claims from the parent cases are as follows:

U.S. Pat. No. 5,354,736

> **1**. A periodontal repair composition comprising:
> hydroxylapatite particles admixed with a quantity of synthetic peptide, the peptide having a domain that mimics collagen binding to cells and has enhanced cell binding with respect to collagen, the peptide in an amount effective to promote cell attachment.

U.S. Pat. No. 5,635,482

> **1**. An implant comprising:
> a matrix formed of a biomaterial and a peptide carried by the matrix, the peptide having enhanced cell binding with respect to collagen, the peptide having a domain that mimics collagen binding to cells, said domain including at least -Ile-Ala- folded in a β-bend at physiologic conditions, wherein the peptide has the sequence Gly-Thr-Pro-Gly-Pro-Gln-Gly-Ile-Ala-Gly-Gln-Arg-Gly-Val-Val (SEQ ID NO: 1), Gly-Pro-Gln-Gly-Ile-Ala-Gly-Gln-Arg (SEQ ID NO: 2), Gln-Gly-Ile-Ala-Gly-Gln (SEQ ID NO: 3), Gln-Gly-Ile-Ala-Gly-Gln-Arg (SEQ ID NO: 4), Phe-Gly-Ile-Ala-Gly-Phe (SEQ ID NO: 5), Gly-Ile-Ala-Gly-Gln (SEQ ID NO: 6), Gln-Gly-Ala-Ile-Ala-Gln (SEQ ID NO: 7), Phe-Gly-Ile-Ala-Gly-Phe (SEQ ID NO:9), Cys-Gly-Ile-Ala-Gly-Cys (SEQ ID NO:10), Glu-Gly-Ile-Ala-Gly-Lys (SEQ ID NO:11), NAc-Ile-Ala-Ala (SEQ ID NO:12), Ile-Ala-βAla (SEQ ID NO:13), and NAc-Ile-Ala-N-Me (SEQ ID NO:14).

U.S. Pat. No. 5,958,428

1. An apparatus for soft tissue repair, comprising:

a biologically compatible structure having interstices or pores; and,

a compound carried on the structure adjacent to the interstices or pores and being in an amount effective to promote cell attachment to the structure and into the interstices or pores, the compound having a domain that mimics collagen binding to cells and having enhanced cell binding with respect to collagen.

4. An apparatus of a construction adapted for cartilage, tendon, or ligament repair, said structure comprising:

a biologically compatible structure including a plurality of fibers; and

a compound carried by the structure, the compound having a domain that mimics collagen binding to cells and has enhanced cell-binding with respect to collagen, the compound being in an amount effective to promote cell attachment to the fibers.

6. A bone repair apparatus, comprising:

a biologically compatible structure including a ceramic, a metal, a polymer or a metal-ceramic composite; and,

a compound carried on the structure and having a domain that mimics collagen binding to cells, and having enhanced cell-binding with respect to collagen, the compound in an amount effective to promote cell attachment to the structure.

10. An additive, useful with medical repair or reconstructive apparatus formed of a biomaterial, the additive including a synthetic peptide, the peptide having a domain that mimics collagen binding to cells and has enhanced cell binding with respect to collagen, the peptide in an amount effective to promote cell attachment when the additive is carried on a repair or reconstructive apparatus wherein the peptide has the sequence Gly-Thr-Pro-Gly-Pro-Gln-Gly-Ile-Ala-Gly-Gln-Arg-Gly-Val-Val (SEQ ID NO: 1), Gly-Pro-Gln-Gly-Ile-Ala-Gly-Gln-Arg (SEQ ID NO: 2), Gln-Gly-Ile-Ala-Gly-Gln (SEQ ID NO: 3), Gln-Gly-Ile-Ala-Gly-Gln-Arg (SEQ ID NO: 4), Phe-Gly-Ile-Ala-Gly-Phe (SEQ ID NO: 5), Gly-Ile-Ala-Gly-Gln (SEQ ID NO: 6), Glu-Gly-Ala-Ile-Ala-Gln (SEQ ID NO: 7), Phe-Gly-Ile-Ala-Gly-Phe (SEQ ID NO: 9), Cys-Gly-Ile-Ala-Gly-Cys (SEQ ID NO: 10), Glu-Gly-Ile-Ala-Gly-Lys (SEQ ID NO: 11), NAc-Ile-Ala-Ala (SEQ ID NO: 12), Ile-Ala-βAla (SEQ ID NO: 13), and NAc-Ile-Ala-N-Me (SEQ ID NO: 14).

U.S. Pat. No. 6,268,348

10. An implant apparatus, comprising:

a biologically compatible structure having interstices or pores, the structure having thereon a compound and living cells growing on the structure, the compound being carried on the structure adjacent to the interstices or pores and being in an amount effective to promote cell attachment to the structure and into the interstices or pores, the compound having a domain that mimics collagen binding to cells and having enhanced cell-binding with respect to collagen.

13. A bone repair apparatus, comprising:

a biologically compatible structure including a ceramic;

a compound carried on the structure, the compound having a domain that mimics collagen binding to cells, and having enhanced cell-binding with respect to collagen, the compound in an amount effective to promote cell attachment to the structure; and,

living cells derived from fibroblasts carried on the structure, wherein the living cells display at least one morphologic change consistent with an oesterogenic phenotype.

15. An apparatus, comprising:
a substrate; and,
a synthetic peptide immobilized on the substrate, the peptide having a domain that mimics collagen binding to cells and having enhanced cell-binding with respect to collagen.

The Office has thus found this same language acceptable repeatedly. Applicants respectfully request withdrawal of this rejection.

Claim 13

Claim 13 was rejected for failure to recite which types of arthritis are encompass by the term "arthritis". This rejection is respectfully traversed.

The term "arthritis" is "inflammation of a joint or a state characterized by inflammation of joints" (see Exhibit 1, which provides an exemplary definition from Stedman's Concise Medical Dictionary for the Health Professions", 1997, JH Dirckx, M.D., Ed. Williams & Wilkins, pg. 74). It is well understood that arthritis can progress to result in damage to the tissues listed in claim 13. The ordinarily skilled artisan would readily understand the meaning of "arthritis" as used in the claim.

Rejection under §112, ¶1

Claim 13 was rejected as not being enabled. This rejection is respectfully traversed.

It is not understood why this rejection is maintained.

The activity of the peptides encompassed by the claim s—as well as several examples of such peptides – are described in the specification. The specification provides several examples showing interaction of cells with a peptide of the claims, including a peptide provided in a biocompatible implant such as a gel (see, e.g., specification page Examples 1- 6, pages 21 - 35).

Applicants presented two separate declarations as further evidence that the peptides have the asserted biological activity *in vivo*.

1) The declaration by Dr. Rajendra S. Bhatnagar (which was filed in a parent application (USSN 08/278,878, now U.S. Pat. No. 5,635,482)), provided a further example of the invention in which an implant of resorbable polymer having P15 is placed at a subcutaneous site in an animal model (Yucutan miniature swine). As a result, the peptides facilitated formation of a well

organized connective tissue, with abundant healthy fibroblasts, in an *in vivo* animal model. The peptide compositions of the invention encourage both cell migration and cell differentiation.

2) In the second declaration, by Andrew J. Tofe, Ph.D. (which declaration was filed in a parent application (USSN 08/278,878, now U.S. Pat. No. 5,635,482)), provided evidence ***that the peptides of the claim can repair damaged tissue in vivo***. The P15 peptide was used to treat a bony defect site in an animal model (NZW rabbits). Dr. Tofe's declaration further evidences that the peptides recited in the present claims provide for repair of bone tissue.

These methods were carried out with a peptide encompassed by the claims, with carriers described in the specification, and using methods described in the specification. It is not understood why, given the above, the enablement rejection should be maintained.

Withdrawal of this rejection is respectfully requested.

Conclusion

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-223CON2.

Respectfully submitted,
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Date: Sept. 2, 2003

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Exhibit 1

STEDMAN'S CONCISE MEDICAL DICTIONARY FOR THE HEALTH PROFESSIONS

ILLUSTRATED / THIRD EDITION

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submental a., *origin*, facial; *distribution*, mylohyoid muscle, submandibular and sublingual glands, and structures of lower lip; *anastomoses*, inferior labial, mental branch of inferior dental and sublingual. SYN arteria submentalis [NA].

subscapular a., *origin*, axillary; *branches*, circumflex scapular, thoracodorsal; *distribution*, muscles of shoulder and scapular region; *anastomoses*, branches of transverse cervical, suprascapular, lateral thoracic, and intercostals. SYN arteria subscapularis [NA].

superficial brachial a., an occasional variation in which the brachial artery lies superficial to the median nerve in the arm.

superior cerebellar a., *origin*, basilar; *distribution*, upper surface of cerebellum, colliculi, and most of the cerebellar nuclei; *anastomoses*, posterior inferior cerebellar.

supraorbital a., *origin*, ophthalmic; *distribution*, frontalis muscle and scalp; *anastomoses*, branches of the superficial temporal and supratrochlear. SYN arteria supraorbitalis [NA].

suprascapular a., *origin*, thyrocervical trunk; *distribution*, clavicle, scapula, muscles of shoulder, and shoulder joint; *anastomoses*, transverse cervical circumflex scapular. SYN arteria suprascapularis [NA], transverse scapular a.

supratrochlear a., *origin*, ophthalmic; *distribution*, anterior portion of scalp; *anastomoses*, branches of supraorbital. SYN arteria supratrochlearis [NA], frontal a.

sural a., one of four or five arteries arising (sometimes by a common trunk) from the popliteal; *distribution*, muscles and integument of the calf; *anastomoses*, posterior tibial, medial, and lateral inferior genicular. SYN arteria suralis [NA].

terminal a., SYN end a.

testicular a., *origin*, aorta; *branches*, ureteral, cremasteric, epididymal; *distribution*, testicle and parts designated by names of branches; *anastomoses*, branches of renal, inferior epigastric, deferential. SYN arteria testicularis [NA].

thoracoacromial a., *origin*, axillary; *distribution*, muscles and skin of shoulder and upper chest; *anastomoses*, branches of superior thoracic, internal thoracic, lateral thoracic, posterior and anterior circumflex humeral, and suprascapular. SYN arteria thoracoacromialis [NA], acromiothoracic a.

thoracodorsal a., *origin*, subscapular; *distribution*, muscles of upper part of back; *anastomoses*, branches of lateral thoracic. SYN arteria thoracodorsalis [NA].

transverse cervical a., *origin*, thyrocervical trunk; *branches*, superficial (superficial cervical) and deep (descending scapular). SYN arteria transversa colli☆ [NA], transverse a. of neck.

transverse facial a., *origin*, superficial temporal; *distribution*, parotid gland, parotid duct, masseter muscle, and overlying skin; *anastomoses*, infraorbital and buccal branches of maxillary, and buccal and masseteric branches of facial. SYN arteria transversa faciei [NA].

transverse a. of neck, SYN transverse cervical a.

transverse scapular a., SYN suprascapular a.

ulnar a., *origin*, brachial; *branches*, ulnar recurrent, common interosseous, dorsal and palmar carpal, deep palmar, and superficial palmar arch with its digital branches. SYN arteria ulnaris [NA].

umbilical a., before birth the a. is a continuation of the internal iliac, after birth it is obliterated between the bladder and umbilicus, forming the medial umbilical ligament, the remaining portion, between the internal iliac artery and bladder, being reduced in size and giving off the superior vesical arteries. SYN arteria umbilicalis [NA].

urethral a., *origin*, perineal artery; *distribution*, membranous urethra. SYN arteria urethralis [NA].

uterine a., *origin*, internal iliac; *distribution*, uterus, upper part of vagina, round ligament, and medial part of uterine (fallopian) tube; *anastomoses*, ovarian, vaginal, inferior epigastric. Supplies maternal circulation to placenta during pregnancy. SYN arteria uterina [NA].

vaginal a., *origin*, internal iliac; *distribution*, vagina, base of bladder, rectum; *anastomoses*, uterine, internal pudendal. SYN arteria vaginalis [NA].

ventricular a.'s, branches of the right and left coronary arteries distributed to the muscle of the ventricles. SYN arteriae ventriculares [NA].

vertebral a., the first branch of the subclavian artery; for descriptive purposes, divided into four parts: 1) prevertebral part, the portion before it enters the foramen of the transverse process of the sixth cervical vertebra; 2) transversarial part, the portion in the transverse foramina of the first six cervical vertebrae; 3) suboccipital (atlantic) part, the portion running along the posterior arch of the atlas; and 4) intracranial part, the portion within the cranial cavity to its union with the artery from the other side to form the basilar artery. SYN arteria vertebralis [NA].

zygomatico-orbital a., *origin*, superficial temporal, sometimes middle temporal; *distribution*, orbicularis oculi muscle and portions of the orbit; *anastomoses*, lacrimal and palpebral branches of ophthalmic. SYN arteria zygomatico-orbitalis [NA].

arthr-. SEE arthro-.

ar•thral•gia (ar-thral′jē-ă). Pain in a joint, especially one not inflammatory in character. SYN arthrodynia. [G. *arthron*, joint, + *algos*, pain]

ar•thral•gic (ar-thral′jik). Relating to or affected with arthralgia. SYN arthrodynic.

ar•threc•to•my (ar-threk′tō-mē). Excision of a joint. [G. *arthron*, joint, + *ektomē*, excision]

ar•thrit•ic (ar-thrit′ik). Relating to arthritis.

ar•thri•tis, pl. **ar•thrit•i•des** (ar-thrī′tis, ar-thrit′i-dēz). Inflammation of a joint or a state characterized by inflammation of joints. SYN articular rheumatism. [G. fr. *arthron*, joint, + *-itis*, inflammation]

atrophic a., obsolete term for a. without new bone formation, now usually called rheumatoid a.

a. defor′mans, SYN rheumatoid a.

gonococcal a., joint space infection in humans caused by disseminated *Neisseria gonorrhoeae*; characteristically monarticular, but may be polyarticular.

gouty a., inflammation of the joints in gout.

hypertrophic a., SYN [illegible] arthritis.

juvenile a., juvenile rheumatoid a., chronic